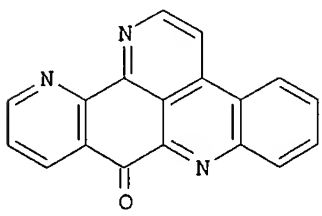
Inventor search

L1 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:208706 CAPLUS
TITLE: Marine pyridoacridine alkaloids and synthetic analogues as antitumor agents
AUTHOR(S): **Delfourne, Evelyne**; Bastide, Jean
CORPORATE SOURCE: Centre de Phytopharmacie, UMR-CNRS 5054, Universite de perpignan, Perpignan, 66860, Fr.
SOURCE: Medicinal Research Reviews (2003), 23(2), 234-252
CODEN: MRREDD; ISSN: 0198-6325
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Pyrido[4,3,4-mn]acridines are of major interest as metabolites in sponges abd ascidians. During the last few years, numerous addnl. compds. of this family were isolated, some of them being polycyclic structures already reported with different substituents (shermilamine or kuanoniamine-derivs.), others, such as neomphimedine, arnoamines and styelsamines having original structures. The synthesis of these compds. and analogs have been performed in order to allow their biologicl evaluation. In most of the cases, the cytotoxicity of analogs was improved compared to the natural product, specially in **ascididemin** or meridine series. The pyridoacridines have not a sole mode of action, but it seems that the reductive DNA cleavage mediated by reactive oxygen species is a potential general mode of action.
REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:525769 CAPLUS
DOCUMENT NUMBER: 137:217121
TITLE: Synthesis and In Vitro Antitumor Activity of Novel Ring D Analogues of the Marine Pyridoacridine **Ascididemin**: Structure-Activity Relationship
AUTHOR(S): **Delfourne, Evelyne**; Darro, Francis; Portefaix, Philippe; Galaup, Chantal; Bayssade, Sylvie; Bouteille, Anne; Le Corre, Laurent; Bastide, Jean; Collignon, Francoise; Lesur, Brigitte; Frydman, Armand; Kiss, Robert
CORPORATE SOURCE: Centre de Phytopharmacie-, UMR-CNRS 5054, Universite de Perpignan, Perpignan, 66860, Fr.
SOURCE: Journal of Medicinal Chemistry (2002), 45(17), 3765-3771
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:217121
GI



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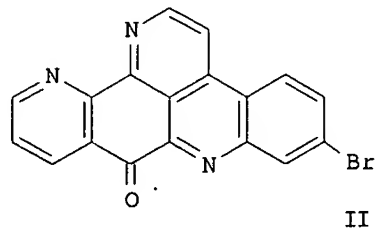

II

AB Marine compds. with pyridoacridine skeletons are known to exhibit interesting antitumor activities. **Ascididemin** has already been reported as displaying significant antitumor activities in vitro and has also been found to have a relatively high global toxicity in vivo. We synthesized a series of 16 analogs (among which 11 compds. were different from previously described ones) with the aim of developing new anticancer agents with significantly improved efficacy/tolerability ratios. These compds. were obtained either by total synthesis from 5,8-quinolinedione and substituted 2-aminoacetophenones or by the direct substitution of **ascididemin** (I). The different compds. and **ascididemin** used as the control compd. were tested at six different concns. on 12 different human cancer cell lines of various histopathol. types (glioblastomas and breast, colon, lung, prostate, and bladder cancers). The IC50 value (i.e., the drug concn. inhibiting the mean growth value of the 12 cell lines by 50%) of these compds. ranged over five log concns., i.e., between 10 000 and 0.1 nM. For several new chem. entities, the antitumor activity (detd. in vitro) and tolerability (detd. in vivo) were superior to those of the parent alkaloids, i.e., **ascididemin** (I) and 2-bromoleptoclinidone (II).

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:137218 CAPLUS
DOCUMENT NUMBER: 134:193607
TITLE: Preparation of phenanthrolin-7-one derivatives and their therapeutic uses as antitumoral medicines
INVENTOR(S): **Delfourne, Evelyne**; Darro, Francis; Bastide, Jean; Kiss, Robert; Frydman, Armand
PATENT ASSIGNEE(S): Laboratoire L. Lafon, Fr.
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001012632	A2	20010222	WO 2000-FR2313	20000811
WO 2001012632	A3	20010719		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2797446	A1	20010216	FR 1999-10493	19990813
FR 2797446	B1	20011102		
BR 2000013239	A	20020423	BR 2000-13239	20000811
EP 1202993	A2	20020508	EP 2000-958679	20000811
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
NO 2002000669	A	20020415	NO 2002-669	20020211

PRIORITY APPLN. INFO.: FR 1999-10493 A 19990813
WO 2000-FR2313 W 20000811

OTHER SOURCE(S): CASREACT 134:193607; MARPAT 134:193607
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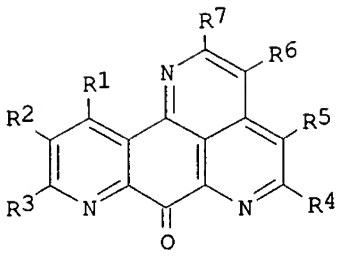

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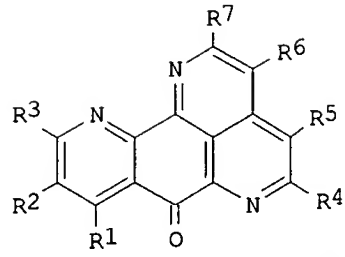

II

AB The invention concerns a pharmaceutical compn. comprising an efficient amt. of a compd. selected among the compds. I [R1, R2, R3, R4, R5 = H, halogen, C1-6-alkyl, OH, CHO, OR8, CO2H, CN, CO2R8, CONHR8, CONR8R9, NH2, NHR8, N(R8)2, NHCH2CH2NMe2, NHCH2CH2Cl, NHCOR8, morpholino, NO2, SO3H, CH2N(CO2R8)CH2CO2R9, CH2N(CO2R8)CH2Ar; R6 = H, halogen, C1-6-alkyl, (CH2)nR10, ; R7 = H, C1-6-alkyl, Ph-C1-4-alkyl, NR15R16; R8, R9 = C1-6-alkyl, Ph-C1-4-alkyl; R10 = halogen, OH, C1-6-alkoxy, OC(:O)-C1-6-alkyl, CN, CO2Et, COR11; R11 = Ph-C1-4-alkyl, NR12R13; R12 , R13 = H, C1-6-alkyl, Ph-C1-4-alkyl, (CH2)nR14; R14 = halogen, C1-6-alkoxy, NMe2; R15, R16 = H, C1-6-alkyl, Ph-C1-4-alkyl, (CH2)nR17; R17 = H, halogen, OH, C1-6-alkoxy; Ar = C6-14-aryl; n = 1 - 6] and II or their pharmaceutically acceptable salts. Thus, I [R1 = R2 = R3 = R4 = R5 = R6 = R7 = H (CRL8293)] and II [R1 = R2 = R3 = R4 = R5 = R6 = R7 = H (CRL8294)] were prepd. from quinoline-5,8-dione via Diels-Alder with crotonaldehyde dimethylhydrazone followed by cyclocondensation of the resulting quinone III with Me2NCMe(OEt)2. I (R1 = R2 = R3 = R4 = R5 = R6 = R7 = H) and II (R1 = R2 = R3 = R4 = R5 = R6 = R7 = H) have interesting cytotoxic properties [DMT = 10 mg/Kg (DMT = max. tolerable dose); -33% and -36%, resp. tumor surface diminution {murin mammary carcinoma (MXT-HI)}; -45% and -64% , resp. tumor surface diminution [{murin mammary adenocarcinoma (MXT-HS)}]; and, for II, T/C = 136% (lymphoma L1210)] leading to a therapeutic use as antitumoral medicines.

L1 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:137217 CAPLUS
DOCUMENT NUMBER: 134:178717
TITLE: **Ascididemin** derivatives and their therapeutic applications
INVENTOR(S): **Delfourne, Evelyne**; Darro, Francis; Bastide, Jean; Kiss, Robert; Frydman, Armand
PATENT ASSIGNEE(S): Laboratoire L. Lafon, Fr.
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001012631	A2	20010222	WO 2000-FR2312	20000811
WO 2001012631	A3	20010719		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,

SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

FR 2797445	A1	20010216	FR 1999-10490	19990813
FR 2797445	B1	20011102		
FR 2809399	A1	20011130	FR 2000-6652	20000524
BR 2000013249	A	20020416	BR 2000-13249	20000811
EP 1202992	A2	20020508	EP 2000-958678	20000811
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003507381	T2	20030225	JP 2001-517529	20000811
NO 2002000668	A	20020415	NO 2002-668	20020211

PRIORITY APPLN. INFO.:	FR 1999-10490	A	19990813
	FR 2000-6652	A	20000524
	WO 2000-FR2312	W	20000811

OTHER SOURCE(S): MARPAT 134:178717

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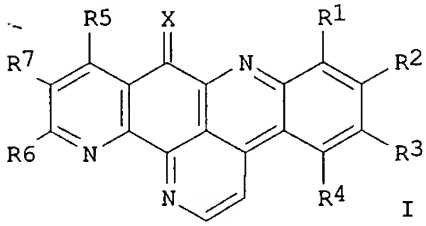

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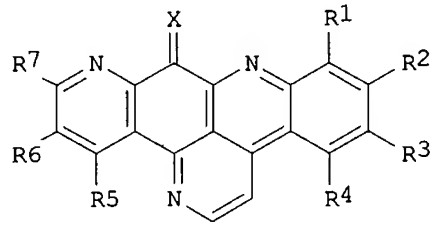

II

AB The invention discloses the prepn. and a pharmaceutical compn. comprising an efficient amt. of a compd. of formulas I and II [R1 = H, halogen, NO2, NR8R9 (R8, R9 = H, alkyl); R2 = H, halogen; R3 = H, halogen, alkyl, alkoxyl etc.; , R4 = H, halogen, NR8R9; R5-R7 = H, halogen, alkyl, carbonyloxyalkyl etc.; X = O, NH, NOH] for use as antitumor agent. Thus, **ascididemin** deriv. I [R1-R2,R4-R7 = H, R3 = Me; X = O] was prepd. via a multistep synthetic sequence starting from quinoline-5,8-dione, 5-methyl-2-amino acetophenone and DMF dimethylacetal. The prepd. **ascididemin** derivs. were tested for cytotoxic properties leading to a therapeutic use of these compds. as antitumoral medicines.